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VALIDATED UV-SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF CAPECITABINE IN BULK AND PHARMACEUTICAL DOSGE FORMULATION

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ABSTRACT

The main aim of this research work is to estimate and validate the capecitabine in the bulk and formulation. Method development was carried out by Lab India-T60, UV/VIS double beam spectrophotometer and matched quartz cells were used for the development of capecitabine. The maximum absorbance of capecitabine was found at 308nm with photo diode array detector. Validation was done according to ICH Q2(R1) guidelines. Linearity for capecitabine was 5-30µg/mL with the correlation coefficient [R^2] 0.999. Accuracy was performed at three concentration levels of 80%, 100% and 120% and the percentage recoveries were found to be within the ranges of 98-102%. Precision results were found to be within the limits of acceptance criteria and method was found to be robust with %RSD limit of NMT 2.0. The LOD and LOQ were found to be 1.0µg/mL and 3.41µg/mL respectively. The method was validated statistically and estimated the capecitabine successfully in the bulk formulations. Hence the proposed method can be applied to routine analysis.

Keywords: Capecitabine, UV spectrophotometer, Validation

INTRODUCTION:

Capecitabine **(Figure 1)**, it is Pentyl N-{1-[(2R,3R,4S,5R)-3,4-dihydroxy-5-methyloxolan-2-yl]-5-fluoro-2-oxo-1,2-dihydropyrimidin-4-yl} carbamate. It has a

molecular formula of $C_{15}H_{22}F\ N_3O_6$ and molecular weight of 359.3501g/mol. capecitabine is an orally-administered chemotherapeutic agent used in the treatment of metastatic breast and colorectal cancers. Capecitabine is a pro-drug that is enzymatically converted to fluorouracil (antimetabolite) in the tumor, where it inhibits DNA synthesis and slows growth of tumor tissue **[1]**.

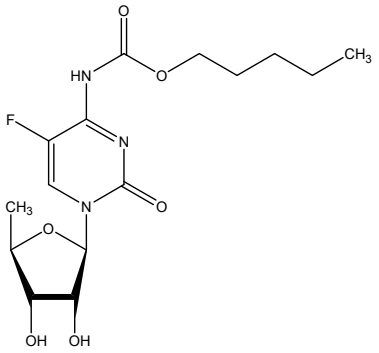

Figure 1: Structure of Capecitabine

MATERIALS AND METHODS:

Instrument:

Lab India-T60, UV/VIS double beam spectrophotometer with spectral band width of 1nm, used for the development of capecitabine.

Chemicals and reagent:

All the reagents were of analytical grade.

METHOD DEVELOPMENT:

Selection of solvent:

Capecitabine is freely soluble in methanol and hence methanol was used as solvent for further preparation of solutions.

Selection of detection wavelength for UV region:

Drug solution of 30µg/mL was scanned over the range of 200-400nm in UV region. It was observed that the drug showed the maximum absorbance at 308nm.

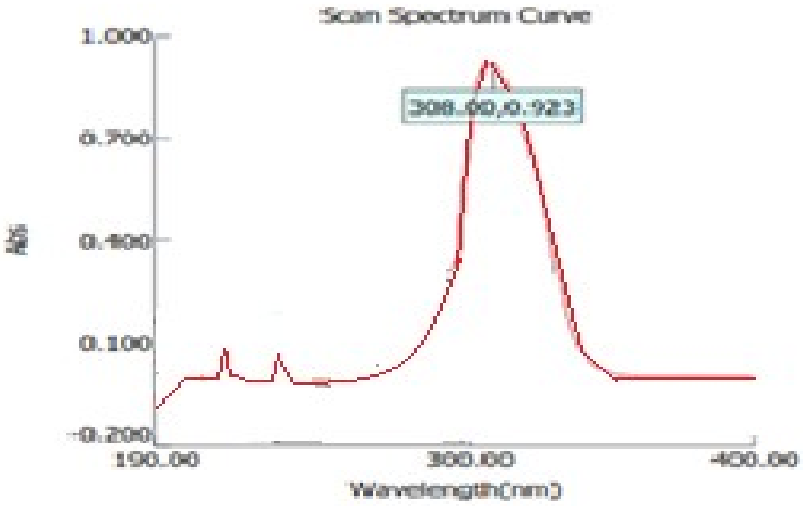

Figure 2: UV Spectrum of Capecitabine

Preparation of standard stock solution:

About 100mg of capecitabine pure drug was accurately weighed and taken into a 100mL volumetric flask and then volume was made up to 100mL with methanol to get 1000µg/mL concentration is called working standard solution.

Preparation of working stock solutions:

From the above standard solution 1mL was pipetted out and made up to 10mL with methanol to obtain 100µg/mL. From the 100µg/mL solution 0.5mL, 1mL, 1.5mL, 2mL, 2.5mL and 3mL solutions were pipetted into a series of six volumetric flasks and made up to 10mL with methanol (5µg/mL, 10µg/mL, 15µg/mL, 20µg/mL, 25µg/mL and 30µg/mL).

Preparation of sample solution:

About 10 tablets were weighed and finely powdered. Powder equivalent to 100mg of drug was weighed and taken into 100mL volumetric flask and then the volume was made up to 100mL with methanol to 1000µg/mL stock sample solution. The 100µg/mL working sample solution was prepared by pipetting 1mL of 1000µg/mL solution into 10mL volumetric flask and filling the remaining volume with methanol.

METHOD VALIDATION:

The proposed method was validated according to the guidelines which includes linearity, accuracy, precision, limit of detection (LOD), limit of quantification (LOQ), Robustness. Under the validation study, the following parameters were studied.

RESULTS:

LINEARITY:

The study was performed over the series of concentration ranging from 5-30µg/mL for Capecitabine. The graphs of concentration v_s absorbance found to be straight line **(Table 1, Figure 3)**.

ACCURACY:

Accuracy test was performed at three different concentration levels of 80%,100%,120% i.e., 12.0,15.0, 18.0µg/mL solutions for UV with three replicates at each level in which the amount of sample was kept constant i.e., 15µg/mL in UV. The percentage recovery, mean, SD, %RSD were calculated for all the 9 readings were found to be within the limits as per ICH guidelines **(Table 2)**.

PRECISION:

The Precision of method was performed by intraday and intraday variations study. The solutions of 20µg/mL in UV were prepared and their absorbance's are noted for the study **(Table 3)**.

LIMIT OF DETECTION (LOD) AND LIMIT OF QUANTIFICATION (LOQ):

LOD and LOQ can be determined by the method as per ICH guide lines. The method is used in this project is based on standard deviation of response and the slope of calibration curve.

The limit of detection was found to be 1.02µg/mL.

The limit of quantification was found to be 3.41µg/mL.

Robustness:

The robustness was performed by taking absorbance of six replicates of 30µg/mL in UV wavelength by ± 1nm of selected wavelength and the results were indicated by % RSD **(Table 4)**.

Table 1: Data of Linearity

S. No	Concentration (µg/mL)	Absorbance
1.	5	0.1276
2.	10	0.2499
3.	15	0.3854
4.	20	0.5039
5.	25	0.6359
6.	30	0.7585

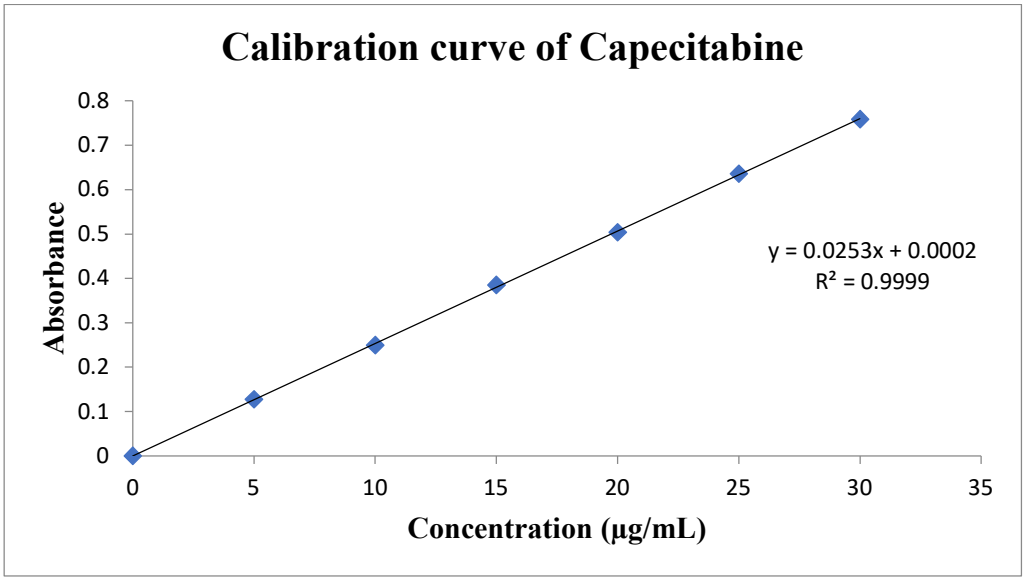

Figure 3: Calibration curve of Capecitabine

Table 2: Data of Accuracy

S. No	Concentration level (%)	Amount added (µg/mL)		Amount found(µg/mL)	% Recovery	Statistical parameters
		Standard	Sample			
1.	80%	12	15	25.95	99.60	Mean-99.43
2.		12	15	25.98	99.20	
3.		12	15	25.96	99.49	
4.	100%	15	15	27.91	99.89	Mean-99.14
5.		15	15	27.95	98.42	
6.		15	15	28.02	99.12	
7.	120%	18	15	30.95	98.45	Mean-98.93
8.		18	15	30.90	99.21	
9.		18	15	30.01	99.14	

Table 3: Data of Precision

Concentration	Sample Set No	% Assay	
		Intraday	Inter day
20µg/mL	1	0.4638	0.4708
	2	0.4625	0.4804
	3	0.4688	0.4627
	4	0.4688	0.4561
	5	0.4625	0.4624
	6	0.4638	0.4626
	Mean	0.4658	0.4660
	SD	0.008528	0.008532
	% RSD	1.83	1.85

Table 4: Data of Robustness

S. No	Concentration (µg/mL)	307nm	308nm	309nm
1	30 µg/mL	0.499	0.500	0.506
2		0.500	0.502	0.508
3		0.502	0.505	0.507
4		0.501	0.502	0.505
5		0.499	0.508	0.506
6		0.504	0.504	0.502
Mean		0.5008	0.503	0.505
SD		0.0014	0.0038	0.0020
%RSD		0.25%	0.74%	0.40%

CONCLUSION:

The developed UV-spectrophotometric method gives a sensitive, accurate, precise and economical results for determination of capecitabine in bulk drug and marketed formulation and easily applied for routine analysis. The economical analytical method was developed for capecitabine. The most striking features of these methods is its simplicity and rapidity. The developed methods were successfully applied for determination of the drug in commercial formulation. The absorbance of capecitabine was measured at 308nm with photo diode array detector. Validation was done according to ICH Q2(R1) guidelines. Linearity for capecitabine was 5-30µg/mL with the correlation coefficient[R^2] 0.999. Accuracy was performed at three concentration levels at80%, 100% and 120% and the results were found to be within the limits of acceptance criteria and percentage recoveries were found to be within the ranges of 98-102%. Precision results were found to be within the limits of acceptance criteria and method was found to be robust with %RSD limit of NMT 2.0. The LOD and LOQ were found to be 1.02µg/mL and 3.41µg/mL respectively. The method was validated statistically and estimated the capecitabine successfully in the bulk formulations. All the parameters like linearity, accuracy, precision, limit of detection, limit of quantification and robustness was within the acceptance limits. Hence the proposed method can be applied to routine analysis.

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REFERENCES:

[1] https://en.wikipedia.org/wiki/Capecitabine

[2] Naveen Kumar, M., Ravi Sankar, Panchumarthy., Srinivasa Babu, Puttagunta., (2013). "Validated UV Spectrophotometric Method for Quantitative Analysis of Capecitabine in Pharmaceutical Dosage Form", J. Chem. and Pharma. Sci. 6(4): Pp. 231-233.

[3] Harini, U., Pawar, A. K. M., (2016). "Validated UV and Visible Spectrophotometric Method for the Estimation of Capecitabine – A cancer drug", Schol. Res. Lib. 8(13): Pp. 11-16

[4] Vijaya Sri, k., Prajawala K., Deepthi S., and Niharika, K., (2018). "Method Development and Validation of UV and RP-HPLC Method for the Estimation of Capecitabine in Bulk and Pharmaceutical Dosage Forms", Asian. J. res. in chem. 11(4): Pp.731-738

[5] Sumanta, Mondal., Reddy, Narendra., Debjit, Ghosh., Seru, Ganapaty., (2016). "Development and validation of RP-HPLC and UV Spectrophotometric for the Quantification of Capecitabine", Int. J. Phar. and Pharma. Sci. 8(5): Pp. 279-287.

[6] Sreenivasa Rao, T., Sukanya, K., Chandanam Sreedhar, Akkamma Hg, Sai Kumar, S., (2012). "Development and Validation of New Analytical Methods for the Estimation of Capecitabine in Pharmaceutical Dosage Form", Res. J. Pharma. Bio and Chem. Sci. 3(3): Pp. 713 – 721.

[7] Pallavi, K., Srinivas Babu, P., Kishore Babu, G., (2016). "Development and Validation of UV Spectrophotometric method and RP-HPLC method for estimation of Capecitabine in Bulk and Tablet Dosage Forms", Int. J. Appli. Pharma. 8(3): Pp. 24-29.